

In re application of  
Wahl and O'Gorman  
Application No.: 10/086,542

Atty. Dkt. No. SALK1790-6 (088802-3457)

### REMARKS

In accordance with the present invention, there are provided transgenic, non-human mammals containing at least one FLP recombination target site in their genomic DNA. FLP transgenic mammals may further contain a nucleotide sequence encoding, and capable of being expressed, an FLP recombinase to effect FLP-mediated recombination. By incorporating an FLP recombination target site, the chromosomal site of transgene integration is controlled, providing a significant advantage over traditional transgenic methodologies that rely on random integration of the transgene. In addition, the level, temporal characteristics, or tissue distribution of transgene expression may be further regulated. For example, specific promoter systems may be used to control FLP recombinase expression, and thus, to control FLP-mediated recombination of a transgene.

By the present communication, claims 1-3 and 12-13 have been amended to define Applicants' invention with greater particularity. These amendments do not add any new matter as they are fully supported throughout the specification and claims as originally filed. In view of these amendments, claim 11 has been cancelled without prejudice.

Upon entry of the amendments to the claims set forth above, claims 1-10 and 12-19 remain pending in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, beginning on page 2 of this paper under "Listing of Claims" with an appropriate defined status identifier.

#### **I. Obviousness-type Double Patenting**

The rejection of claims 1-19 under the judicially created doctrine of obviousness-type double patenting is respectfully traversed. Applicants respectfully disagree with the Examiner's assertion that the claims of U.S. Patent No. 5,677,177 encompass the claims of the instant

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application (Office Action, page 2), for at least the reasons of record. However, in the interest of advancing prosecution and reducing issues, a terminal disclaimer is provided herewith.

## **II. 35 U.S.C. §112, 1<sup>st</sup> Paragraph (Enablement)**

The rejection of claims 1-19 under 35 U.S.C. § 112, first paragraph for alleged lack of enablement is respectfully traversed. Applicants respectfully disagree with the Examiner's assertion that the specification allegedly does not provide enablement for any FLP recombination target site as encompassed by the claims. Applicants respectfully submit that the specification provides both structural and functional information which describes an FLP recombination target site contemplated for use herein, thereby fully enabling the claims.

Indeed, as acknowledged by the Examiner, the specification is enabling for a transgenic mammal wherein the mammal contains an FLP recombination target site in its genomic DNA wherein the FLP recombination target site comprises two 13-base pair repeats separated by a random 8-base pair spacer as in SEQ ID NO:3 (Office Action, page 3).

Accordingly, in order to reduce the issues and expedite prosecution, claim 1, as amended herein, defines the FLP recombination target site consistently with that which has been acknowledged by the Examiner to have been enabled. In view of the amendments submitted herewith, reconsideration and withdrawal of this rejection are respectfully requested.

## **III. 35 U.S.C. §112, 2<sup>nd</sup> Paragraph**

### **A. Claims 2, 9, 10, 12, 13, and 17-19.**

The rejection of claims 2, 9, 10, 12, 13, and 17-19 under 35 U.S.C. § 112, second paragraph on the grounds that claim 2 is allegedly unclear, is respectfully traversed. Applicants respectfully disagree with the Examiner's assertion that the phrase "one or more genes of

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interest" is allegedly unclear on the grounds that it is unclear how an FLP recombination target site can be incorporated into more than one gene (Office Action, page 6).

Applicants respectfully submit that it is quite possible for an FLP recombination target site to be positioned within more than one gene when two genes overlap. Recently, a report by Veeramachaneni et al. (Genome Research 14:280-286, 2000, copy provided herewith for the Examiner's convenience) suggested that there are over 700 pairs of overlapping genes in the human genome and over 500 pairs of overlapping genes in the mouse genome (see Table 1 of Veeramachaneni). This reference further cites reports of overlapping genes in the human genome which date back to the late 1980's. Therefore, it is clear that it is possible for an FLP recombination target site to be positioned within more than one gene if it should integrate into a region in which two genes overlap. Moreover, one of skill in the art would have recognized, at the time of filing of the instant application, how this would be possible.

However, in the interest of advancing prosecution and reducing issues, claim 2 has been amended herein to replace the phrase "one or more gene(s) of interest" with the phrase "a first gene of interest."

Applicants further disagree with the Examiner's assertion that it is not clear what makes a gene "of interest" (Office Action, page 6). Applicants respectfully submit that the phrase "gene of interest" is clear and would be clear to one of skill in the art. First, genes of interest are discussed throughout the specification (e.g., see paragraph [0030] for examples of genes of interest). Second, the phrase "gene of interest" is widely used by those of skill in the art and would be readily understood to be a gene which one is studying. Finally, Applicants respectfully note that the phrase "gene of interest" is present in the claims of three issued patents (U.S. Patent No. 5,654,182, U.S. Patent No. 5,677,177, and U.S. Patent No. 5,885,836) from the same family as the instant application.

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**B. Claims 3 and 15**

The rejection of claims 3 and 15 under 35 U.S.C. §112, second paragraph, as allegedly being unclear is respectfully traversed. Applicants respectfully disagree with the Examiner's assertion that the phrase "a nucleotide sequence encoding, and capable of expressing" in claim 3 is unclear (Office Action, page 6). Contrary to the Examiner's assertion, Applicants respectfully submit that claim 3 is clear as presented. However in the interest of advancing prosecution and reducing issues, claim 3 has been amended herein to replace the above phrase with the phrase "a nucleotide sequence encoding, and capable of being expressed."

**C. Claims 13 and 14**

The rejection of claims 13 and 14 under 35 U.S.C. §112, second paragraph, as allegedly being unclear is respectfully traversed. Applicants respectfully disagree with the Examiner's assertion that it is unclear as to which gene "said gene of interest" in claim 13 refers (Office Action, page 6). Contrary to the Examiner's assertion, Applicants respectfully submit that claim 13 is clear as presented. However in the interest of advancing prosecution and reducing issues, claim 13 has been amended herein to replace the phrase "said gene of interest" with the phrase "said first gene of interest."

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### CONCLUSION

In view of the above amendments and remarks, the present application is respectfully submitted to be in condition for allowance. Accordingly, reconsideration and favorable action with respect to the pending claims is respectfully requested. In the event any issues remain to be resolved in view of this communication, the Examiner is invited to contact the undersigned at the number given below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

Date. 12/14/04

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Enclosure: Terminal Disclaimer  
Veeramachaneni et al. (Genome Research 14:280-286, 2000)